Commentary
Volume 13:02, 2025

Journal of Clinical & Medical Genomics

ISSN: 2472-128X

Open Access

Leveraging Polygenic Risk Scores to Optimize Pharmacogenomics and Drug Response Prediction

Clinton Chen*

Department of Urology, Columbia University, New York, USA

Introduction

The landscape of modern medicine is undergoing a profound transformation fueled by advances in genomics, data science, and personalized healthcare. One of the most promising frontiers in this revolution is the integration of genetic information into pharmacotherapy to tailor drug selection and dosing to individual patients. Pharmacogenomics, the study of how genetic variation affects drug response, has long held the promise of reducing adverse drug reactions and improving therapeutic outcomes. Traditionally, pharmacogenomics has focused on identifying specific single-gene variants that influence drug metabolism, transport, and receptor activity. Examples include the impact of CYP2D6 on codeine metabolism, VKORC1 and CYP2C9 on warfarin sensitivity, and HLA-B*57:01 on abacavir hypersensitivity. While these pharmacogenetic markers have been successfully implemented in clinical settings, they represent only a fraction of the genetic architecture underlying interindividual variability in drug response.

Description

Emerging evidence suggests that complex drug responses often involve the interplay of multiple genetic variants across the genome, each contributing modestly to the phenotype. This polygenic architecture mirrors what has been observed in complex diseases like diabetes, cardiovascular disease, and psychiatric disorders. Consequently, researchers have begun to explore the utility of Polygenic Risk Scores (PRS)—aggregated measures of genetic liability calculated from Genome-Wide Association Study (GWAS) data—as tools to capture this complexity. PRS are typically derived by summing risk alleles across many Single-Nucleotide Polymorphisms (SNPs), weighted by their effect sizes estimated from GWAS. The result is a single quantitative measure that reflects an individual's inherited predisposition to a given trait or outcome. While PRS have primarily been applied to disease risk prediction, their application to pharmacogenomics represents a compelling and underexplored domain that could significantly advance precision medicine [1].

Integrating PRS into pharmacogenomics offers several conceptual and practical advantages. First, PRS can capture a broader spectrum of genetic influences than traditional single-gene pharmacogenetic markers. For many drugs, especially those used in treating multifactorial conditions, response and adverse effects are influenced by numerous small-effect variants rather than a few high-impact ones [2]. For example, the response to statins, antidepressants, and antihypertensives is only partially explained by known pharmacokinetic and pharmacodynamic genes. PRS can complement these markers by accounting for additional genomic contributions, including those related to underlying disease susceptibility or relevant physiological pathways. In this way, PRS can serve as an integrative measure that bridges pharmacogenomics and disease genomics, providing a more comprehensive picture of individual variability in drug response [3].

Second, PRS can be used to stratify patients by their likelihood of responding to a particular therapy or experiencing side effects. This stratification can inform drug selection, dosing strategies, and monitoring plans [4]. For instance, in psychiatric treatment, where drug efficacy is often unpredictable and adverse effects are common, PRS for schizophrenia, depression, or bipolar disorder could potentially identify individuals more likely to respond to specific antipsychotics or antidepressants. Pilot studies have already indicated associations between higher schizophrenia PRS and greater benefit from clozapine, an antipsychotic reserved for treatment-resistant cases. Similarly, in oncology, PRS for breast cancer subtypes may one day help determine which patients are likely to benefit from hormone therapy versus chemotherapy. These applications underscore the utility of PRS as predictive biomarkers for therapeutic decision-making [5].

Conclusion

In conclusion, leveraging polygenic risk scores to optimize pharmacogenomics and drug response prediction represents an exciting and transformative opportunity in the evolution of precision medicine. By capturing the complex, polygenic architecture of drug response, PRS can enhance the accuracy of treatment selection, reduce adverse drug reactions, and increase therapeutic efficacy across a wide range of clinical conditions. Although substantial scientific, technical, and ethical challenges remain, the integration of PRS into pharmacogenomics is both feasible and increasingly supported by emerging research. Realizing this potential will require continued investment in large, diverse genomic cohorts, methodological innovation, clinician and patient education, and robust policy frameworks to ensure equitable and ethical implementation. As these elements come together, PRS-guided pharmacotherapy promises to move the field closer to a future in which medical treatment is precisely tailored to each individual's unique genetic makeup, improving outcomes and reshaping how medicine is practiced in the genomic era.

Acknowledgment

None.

Conflict of Interest

None.

References

1. Wray, Naomi R., Michael E. Goddard and Peter M. Visscher. "Prediction of individual genetic risk to disease from genome-wide association studies." *Genome Res* 17 (2007): 1520-1528.

***Address for Correspondence:** Clinton Chen, Department of Urology, Columbia University, New York, USA; E-mail: chen.clinton@gmail.com*

Received: 01 April, 2025, Manuscript No. JCMG-25-165761; **Editor assigned:** 03 April, 2025, Pre QC No. P-165761; **Reviewed:** 17 April, 2025, QC No. Q-165761; **Revised:** 22 April, 2025, Manuscript No. R-165761; **Published:** 29 April, 2025, DOI: 10.37421/2472-128X.2025.13.331

2. Alfirevic, Ana and Munir Pirmohamed. "Genomics of adverse drug reactions." *Trends Pharmacol Sci* 38 (2017): 100-109.

3. Mavaddat, Nasim, Kyriaki Michailidou, Joe Dennis and Michael Lush, et al. "Polygenic risk scores for prediction of breast cancer and breast cancer subtypes." *Am J Hum Genet* 104 (2019): 21-34.

4. Auwerx, Chiara, Marie C. Sadler, Alexandre Reymond and Zoltán Kutalik. "From pharmacogenetics to pharmaco-omics: Milestones and future directions." Hum *Genet Genom Adv* 3 (2022).

5. Daly, Ann K. "Genome-wide association studies in pharmacogenomics." *Nat Rev Genet* 11 (2010): 241-246.

How to cite this article: Chen, Clinton. "Leveraging Polygenic Risk Scores to Optimize Pharmacogenomics and Drug Response Prediction." *J Clin Med Genomics* 13 (2025): 331.